

*a<sup>2</sup>*  
*contd*

26. (amended) A pharmaceutical composition according to claim 23 wherein the  $\beta_3$  agonist is N-[(2S)-7-ethoxycarbonylmethoxy-1,2,3,4-tetrahydronaphth-2-yl]-(2R)-2-(3-chlorophenyl)-2-hydroxyethanamine or one of its pharmaceutically acceptable salts.

27. (amended) A pharmaceutical composition according to claim 23 containing from 0.5 to 600 mg of CB<sub>1</sub> receptor antagonist and from 0.5 to 600 mg of  $\beta_3$ -agonist.

*a<sup>3</sup>*

32. (amended) A kit according to claim 31 in which said CB<sub>1</sub> receptor antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide, one of its pharmaceutically acceptable salts or one of their solvates and said  $\beta_3$ -agonist is N-[(2S)-7-ethoxycarbonylmethoxy-1,2,3,4-tetrahydronaphth-2-yl]-(2R)-2-(3-chlorophenyl)-2-hydroxyethanamine or one of its pharmaceutically acceptable salts.

33. (amended) A kit according to claim 30 in which said active principles are in different packagings.

Please add the following new claim:

*a<sup>4</sup>*

39. (added) A pharmaceutical composition according to claim 26 wherein the CB<sub>1</sub> antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide or one of its pharmaceutically acceptable salts or one of their solvates.

#### REMARKS

The specification has been amended in order to provide the appropriate cross-reference to related application information.

Claims 1-18 and 34-38, which are directed to the subject matter which was elected for prosecution and allowed in U.S. application Serial No. 09/341,764, have been canceled.

Claims 19-27 and 32-33 have been rewritten in accordance with U.S. practice, and multiple dependencies have been eliminated from claims 21, 23-27 and 32-33.

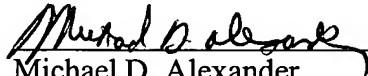
New claim 39 is directed to a pharmaceutical composition containing the preferred CB<sub>1</sub> antagonist and B<sub>3</sub> agonist recited separately in composition claims 22 and 26, respectively.

Claims 19-33 and 39 remain in the application

Attached hereto is a marked-up version of the changes made to the specification and claims by the instant amendment. The marked-up version is entitled "Version With Markings To Show Changes Made".

Respectfully submitted,

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**Version With Markings to Show Changes Made**

**In the specification**

On page 1, after the title of the invention and before line 2 insert the following cross reference to related application section was inserted:

**--Cross Reference to Related Applications**

This application is a divisional of prior copending application, Serial No. 09/341,764, filed August 19, 1999, which in turn is a 35 U.S.C. 371 application of PCT International application No. PCT/FR98/00154, filed January 28, 1998, which in turn claims priority from French application No. 97/00870, filed January 28, 1997.--

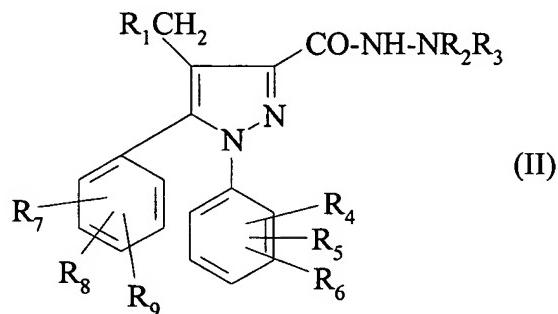
**In the Claims:**

Claims 19-27 and 32-33 have been amended as follows:

19. (amended) A pharmaceutical composition containing a CB<sub>1</sub> receptor antagonist and a regulator of metabolic functions together with a pharmaceutical excipient.

20. (amended) A pharmaceutical composition according to claim 19[, characterized in that] wherein said regulator of metabolic functions is a β<sub>3</sub>-agonist.

21. (amended) A pharmaceutical composition according to claim [19 or] 20[, characterized in that] wherein the CB<sub>1</sub> receptor antagonist is a compound of the formula



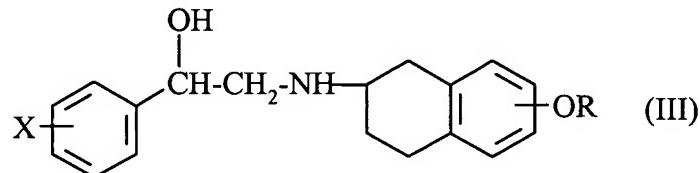
in which:

- R<sub>1</sub> is hydrogen, a fluorine, a hydroxyl, a (C<sub>1</sub>-C<sub>5</sub>)alkoxy, a (C<sub>1</sub>-C<sub>5</sub>)alkylthio, a hydroxy(C<sub>1</sub>-C<sub>5</sub>)alkoxy, a group -NR<sub>10</sub>R<sub>11</sub>, a cyano, a (C<sub>1</sub>-C<sub>5</sub>)alkylsulfonyl or a (C<sub>1</sub>-C<sub>5</sub>)alkylsulfinyl;

- R<sub>2</sub> and R<sub>3</sub> are a (C<sub>1</sub>-C<sub>4</sub>)alkyl or, together with the nitrogen atom to which they are bonded, form a saturated or unsaturated 5- to 10-membered heterocyclic radical which is unsubstituted or monosubstituted or polysubstituted by a (C<sub>1</sub>-C<sub>3</sub>)alkyl or by a (C<sub>1</sub>-C<sub>3</sub>)alkoxy;
  - R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> and R<sub>9</sub> are each independently hydrogen, a halogen or a trifluoromethyl, and if R<sub>1</sub> is a fluorine, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> and/or R<sub>9</sub> can also be a fluoromethyl, with the proviso that at least one of the substituents R<sub>4</sub> or R<sub>7</sub> is other than hydrogen;
  - R<sub>10</sub> and R<sub>11</sub> are each independently hydrogen or a (C<sub>1</sub>-C<sub>5</sub>)alkyl, or R<sub>10</sub> and R<sub>11</sub>, together with the nitrogen atom to which they are bonded, form a heterocyclic radical selected from pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl and piperazin-1-yl, which is unsubstituted or substituted by a (C<sub>1</sub>-C<sub>4</sub>)alkyl,
- one of its salts or one of their solvates.

22. (amended) A pharmaceutical composition according to claim 21[, characterized in that] wherein the CB<sub>1</sub> receptor antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide, one of its pharmaceutically acceptable salts or one of their solvates.

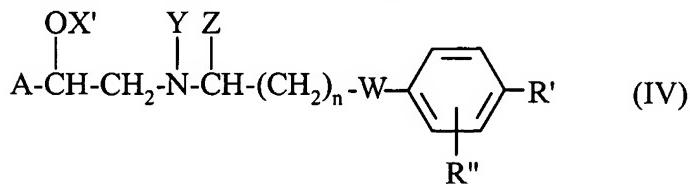
23. (amended) A pharmaceutical composition according to [any one of claims 20 to 22, characterized in that] claim 21 wherein the β<sub>3</sub>-agonist is a compound of the formula



in which:

- X is hydrogen, a halogen, a trifluoromethyl or a (C<sub>1</sub>-C<sub>4</sub>)alkyl;
  - R is hydrogen or a methyl which is unsubstituted or substituted by a carboxyl or an alkoxy carbonyl in which the alkoxy is (C<sub>1</sub>-C<sub>6</sub>),
- or one of its pharmaceutically acceptable salts.

24. (amended) A pharmaceutical composition according to [any one of claims 20 to 22, characterized in that] claim 21 wherein the  $\beta_3$ -agonist is a compound of the formula



in which:

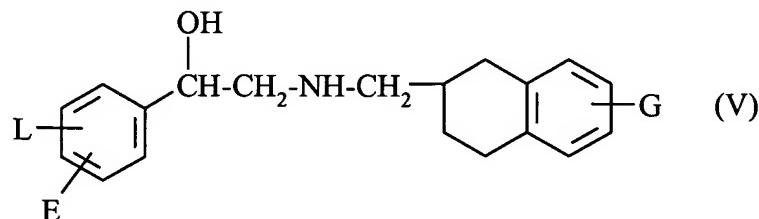
- n is 1, 2 or 3;
- A is a benzofuran-2-yl or a phenyl which is unsubstituted or substituted by one or two halogen atoms or by a (C<sub>1</sub>-C<sub>4</sub>)alkyl or a trifluoromethyl;
- R' is:
  - hydrogen;
  - a (C<sub>1</sub>-C<sub>6</sub>)alkyl;
  - a functional group selected from the following groups: hydroxyl; (C<sub>1</sub>-C<sub>6</sub>)alkoxy; (C<sub>2</sub>-C<sub>6</sub>)alkenyloxy; (C<sub>2</sub>-C<sub>6</sub>)alkynyloxy; (C<sub>3</sub>-C<sub>8</sub>)cycloalkoxy; (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkoxy; benzyloxy; phenoxy; mercapto; (C<sub>1</sub>-C<sub>6</sub>)alkylthio; (C<sub>2</sub>-C<sub>6</sub>)alkenylthio; (C<sub>2</sub>-C<sub>6</sub>)alkynylthio; (C<sub>3</sub>-C<sub>8</sub>)cycloalkylthio; (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkylthio; benzylthio; phenylthio; (C<sub>1</sub>-C<sub>6</sub>)alkylsulfinyl; (C<sub>2</sub>-C<sub>6</sub>)alkenylsulfinyl; (C<sub>2</sub>-C<sub>6</sub>)alkynylsulfinyl; (C<sub>3</sub>-C<sub>8</sub>)cycloalkylsulfinyl; (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkylsulfinyl; benzylsulfinyl; phenylsulfinyl; (C<sub>1</sub>-C<sub>6</sub>)alkylsulfonyl; (C<sub>2</sub>-C<sub>6</sub>)alkenylsulfonyl; (C<sub>2</sub>-C<sub>6</sub>)alkynylsulfonyl; (C<sub>3</sub>-C<sub>8</sub>)cycloalkylsulfonyl; (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkylsulfonyl; benzylsulfonyl; phenylsulfonyl; cyano; nitro; amino which is unsubstituted or substituted by one or two identical or different radicals selected from (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>2</sub>-C<sub>6</sub>)alkynyl, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, benzyl and phenyl groups; carboxyl; alkoxy carbonyl in which the alkoxy is (C<sub>1</sub>-C<sub>6</sub>); (C<sub>2</sub>-C<sub>6</sub>)alkenyloxycarbonyl; (C<sub>2</sub>-C<sub>6</sub>)alkynyloxycarbonyl; (C<sub>3</sub>-C<sub>8</sub>)cycloalkoxycarbonyl; (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl; benzyloxycarbonyl; phenoxy carbonyl; and carbamoyl which is unsubstituted or

substituted on the amino group by one or two identical or different radicals selected from (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>2</sub>-C<sub>6</sub>)alkynyl, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, benzyl and phenyl groups;

- a group R''' selected from the following groups: (C<sub>1</sub>-C<sub>6</sub>)alkyl substituted by a functional group; (C<sub>2</sub>-C<sub>6</sub>)alkenyl substituted by a functional group; (C<sub>2</sub>-C<sub>6</sub>)alkynyl substituted by a functional group; phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl substituted on the phenyl by a (C<sub>1</sub>-C<sub>6</sub>)alkyl or by a functional group; phenyl(C<sub>2</sub>-C<sub>6</sub>)alkenyl substituted on the phenyl by a (C<sub>1</sub>-C<sub>6</sub>)alkyl or by a functional group; phenyl(C<sub>2</sub>-C<sub>6</sub>)alkynyl substituted on the phenyl by a (C<sub>1</sub>-C<sub>6</sub>)alkyl or by a functional group; benzyl substituted on the phenyl by a (C<sub>1</sub>-C<sub>6</sub>)alkyl or by a functional group; and phenyl which is unsubstituted or substituted by a (C<sub>1</sub>-C<sub>6</sub>)alkyl or by a functional group, the functional group being as defined above;
- a group O-R''', S-R''', SO-R''' or SO<sub>2</sub>-R''', in which R''' is as defined above;
- a group NR'''R°, in which R''' is as defined above and R° is hydrogen or is as defined above for R''', or R''' and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- a group COOR''' or a group CO-SR''', in which R''' is as defined above;
- a group CONR'''R°, in which R''' is as defined above and R° is hydrogen or is as defined above for R''', or R''' and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- a group SO<sub>2</sub>NR'''R°, in which R''' is as defined above and R° is hydrogen or is as defined above for R''', or R''' and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- R'' is hydrogen; a halogen; a (C<sub>1</sub>-C<sub>6</sub>)alkyl; a functional group as defined above; a group OR''', R''' being as defined above; a group COOR''', R''' being as defined above; or a group CONR'''R°, in which R''' is as defined above and R° is hydrogen or is as defined above for R''', or R''' and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- W is a direct bond or an oxygen atom;
- X' is hydrogen, a (C<sub>1</sub>-C<sub>6</sub>)alkyl or a (C<sub>1</sub>-C<sub>6</sub>)alkylcarbonyl;

- Y is hydrogen or a group A'-CH(OH)-CH<sub>2</sub>-, A' being identical to A but other than benzofuran-2-yl; or
- X' and Y, taken together, form a methylene group optionally substituted by an alkoxy carbonyl in which the alkoxy is (C<sub>1</sub>-C<sub>6</sub>); an ethylene group optionally substituted by an oxo group; or a 1,3-propylene group;
- Z is hydrogen or a (C<sub>1</sub>-C<sub>6</sub>)alkyl,  
or one of its pharmaceutically acceptable salts.

25. (amended) A pharmaceutical composition according to [any one of claims 20 to 22]  
claim 21 wherein the β<sub>3</sub>-agonist is a compound of the formula



in which:

- E is hydrogen, a (C<sub>1</sub>-C<sub>4</sub>)alkyl, a (C<sub>1</sub>-C<sub>4</sub>)alkoxy, a phenyl, a nitro, a halogen atom or a trifluoromethyl;
- L is hydrogen, a (C<sub>1</sub>-C<sub>4</sub>)alkyl, a (C<sub>1</sub>-C<sub>4</sub>)alkoxy, a phenyl, a nitro or a halogen atom; or E and L together are a group -CH=CH-CH=CH- or -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-; and
- G is hydrogen, a chlorine atom, a hydroxyl or a group OG', in which G' is a (C<sub>1</sub>-C<sub>4</sub>)alkyl which is unsubstituted or substituted by a hydroxyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy, (C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl, carboxyl or (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl; a (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl; or a (C<sub>2</sub>-C<sub>4</sub>)alkanoyl,

or one of its pharmaceutically acceptable salts.

26. (amended) A pharmaceutical composition according to claim 23[, characterized in that] wherein the β<sub>3</sub> agonist is N-[(2S)-7-ethoxycarbonylmethoxy-1,2,3,4-tetrahydronaphth-2-yl]-(2R)-2-(3-chlorophenyl)-2-hydroxyethanamine or one of its pharmaceutically acceptable salts.

27. (amended) A pharmaceutical composition according to [any one of claims 20 to 26] claim 23 containing from 0.5 to 600 mg of CB<sub>1</sub> receptor antagonist and from 0.5 to 600 mg of β<sub>3</sub>-agonist.

32. (amended) A kit according to claim [30 or] 31 in which said CB<sub>1</sub> receptor antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide, one of its pharmaceutically acceptable salts or one of their solvates and said β<sub>3</sub>-agonist is N-[(2S)-7-ethoxycarbonylmethoxy-1,2,3,4-tetrahydronaphth-2-yl]-(2R)-2-(3-chlorophenyl)-2-hydroxyethanamine or one of its pharmaceutically acceptable salts.

33. (amended) A kit according to [any one of claims 30 to 32] claim 30 in which said active principles are in different packagings.

Claims 1-18 and 34-38 have been canceled.

New claim 39 has been added.